CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

75-547

ADMINISTRATIVE DOCUMENTS

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

APPLICATION TO MARKET A NEW DRUG, BIOLOGIC, OR AN ANTIBIOTIC DRUG FOR HUMAN USE

(Title 21, Code of Federal Regulations, 314 & 601)

Form Approved OMB No. 0910-0338
Expiration Date: March 31, 2003
See OMB Statement on last page

FOR FDA USE ONLY

APPLICATION NUMBER

APPLICANT INFORMATION

NAME OF APPLICANT Bedford Laboratories™ (A Division of Ben Venue Laboratories, Inc.)	DATE OF SUBMISSION March 1, 2001
TELEPHONE NO. *(Include Area Code)* (440) 201-3333	FACSIMILE (FAX) Number *(Include Area Code)* (440) 232-2772
APPLICANT ADDRESS (Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued): 300 Northfield Road Bedford, Ohio 44146	AUTHORIZED U.S. AGENT NAME & ADDRESS (Number, Street, City, State, Country, ZIP Code, telephone & FAX number) IF APPLICABLE N/A

PRODUCT DESCRIPTION

NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER, OR BIOLOGIC LICENSE APPLICATION NUMBER *(if previously issued)* 75-547

ESTABLISHED NAME (e.g., Proper name, USP/USAN name) Thiotepa for Injection, USP	PROPRIETARY NAME (trade name) IF ANY
CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME Tris(1-aziridinyl)phosphine sulfide	CODE NAME *(if any)* Thioplex®

DOSAGE FORM: Lyophilized	STRENGTHS: 15 mg per vials	ROUTE OF ADMINISTRATION: Intravenous, Intracavitary, Intravesical

(PROPOSED) INDICATION(S) FOR USE: Has been tried with varying results in the palliation of a wide variety of neoplastic diseases.

APPLICATION INFORMATION

APPLICATION TYPE
(check one) ☐ NEW DRUG APPLICATION (21 CFR 314.50) X ☐ ABBREVIATED NEW DRUG APPLICATION (ANDA 21 CFR 314.94)
☐ BIOLOGIC LICENSE APPLICATION (21 CFR PART 601)

IF AN NDA, IDENTIFY THE APPROPRIATE TYPE ☐ 505(b) (1) ☐ 505 (b)(2)

IF AN ANDA, OR 505(B) (2), IDENTIFY THE REFERENCED LISTED DRUG PRODUCT THAT IS THE BASIS FOR THE SUBMISSION

Name of Drug	Holder of Approved Application
Thioplex®	Immunex®

TYPE OF SUBMISSION (check one) ☐ ORIGINAL APPLICATION X ☐ AMENDMENT TO A PENDING APPLICATION ☐ RESUBMISSION
☐ PRESUBMISSION ☐ ANNUAL REPORT ☐ ESTABLISHMENT DESCRIPTION SUPPLEMENT
☐ EFFICACY SUPPLEMENT ☐ LABELING SUPPLEMENT ☐ CHEMISTRY MANUFACTURING AND CONTROLS SUPPLEMENT ☐ OTHER

IF A SUBMISSION OF PARTIAL APPLICATION, PROVIDE LETTER DATE OF AGREEMENT TO PARTIAL SUBMISSION: _____

IF A SUPPLEMENT, IDENTIFY THE APPROPRIATE CATEGORY ☐ CBE ☐ CBE-30 ☐ Prior Approval (PA)

REASON FOR SUBMISSION: Telephone Amendment

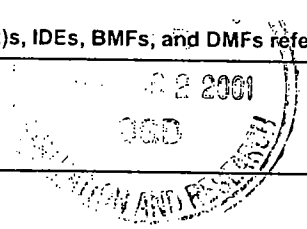
PROPOSED MARKETING STATUS (check one) X ☐ PRESCRIPTION PRODUCT (Rx) ☐ OVER THE COUNTER PRODUCT (OTC)

NUMBER OF VOLUMES SUBMITTED: One	THIS APPLICATION IS X ☐ PAPER ☐ PAPER AND ELECTRONIC ☐ ELECTRONIC

ESTABLISHMENT INFORMATION (Full establishment information should be provided in the body of the Application.) Provide locations of all manufacturing, packaging and control sites for drug substance and drug product (continuation sheets may be used if necessary). Include name, address, contact, telephone number, registration number (CFN), DMF number, and manufacturing steps and/ or type of testing (e.g., Final dosage form, Stability testing) conducted at the site. Please indicate whether the site is ready for inspection or, if not, when it will be ready.

Drug Product Manufacturer: Ben Venue Laboratories, Inc., 300 Northfield Road, Bedford, OH 44146, Registration Number - 1519257

Cross Reference (list related License Applications, INDs, NDAs, PMAs, 510(k)s, IDEs, BMFs, and DMFs reference in the current application).



This application contains the following items: (*Check all that apply*)

	1. Index
	2. Labeling (check one) ☐ Draft Labeling ☐Final Printed Labeling
	3. Summary (21 CFR 314.50(c))
X	4. Chemistry section
	A. Chemistry, manufacturing, and controls information (e.g., 21 CFR 314.50 (d)(1), 21 CFR 601.2)
	B. Samples (21 CFR 314.50(e)(1), 21 CFR 601.2(a)) (Submit only upon FDA's request)
	C. Methods validation package (e.g., 21 CFR 314.50(e)(2)(i), 21 CFR 601.2)
	5. Nonclinical pharmacology and toxicology section (e.g., 21 CFR 314.50(d)(2), 21 CFR 601.2)
	6. Human pharmacokenitics and bioavailibility section (e.g., 21 CFR 314.50(d)(3), 21 CFR 601.2)
	7. Clinical Microbiology (e.g., 21 CFR 314.50(d)(4))
	8. Clinical data section (e.g., 21 CFR 314.50(d)(5), 21 CFR 601.2)
	9. Safety update report (e.g., 21 CFR 314.50(d)(5)(vi), 21 CFR 601.2)
	10. Statistical section (e.g., 21 CFR 314.50(d)(6), 21 CFR 601.2)
	11. Case report tabulations (e.g., 21 CFR 314.50(f)(1), 21 CFR 601.2)
	12. Case report forms (e.g., 21 CFR 314.50(f)(2), 21 CFR 601.2)
	13. Patent information on any patent which claims the drug (21 U.S.C. 3555 (b) or (c))
	14. A patent certification with respect to any patent which claims the drug (21 U.S.C. 355(b)(2) or (j)(2)(A))
	15. Establishment description (21 CFR Part 600, if applicable)
	16. Debarment certification (FD&C Act 306 (k)(1))
	17. Field copy certification (21 CFR 314.5(k)(3))
	18. User Fee Cover Sheet (Form FDA 3397)
	19. Financial Information (21 CFR Part 54)
	19. Other (Specify)

CERTIFICATION

I agree to update this application with new safety information about the product that may reasonably affect the statement of contraindications, warnings, precautions, or adverse reactions in the draft labeling. I agree to submit safety update reports as provided for by regulation or as requested by FDA. If this application is approved, I agree to comply with all applicable laws and regulations that apply to approved applications, including, but not limited to the following:

1. Good manufacturing practice regulations in 21 CFR 210 and 211, 606, and/or 820.
2. Biological establishment standards in 21 CFR 600.
3. Labeling regulations in 21 CFR 201, 606, 610, 660 and/or 809.
4. In the case of a prescription drug or biological product, prescription drug advertising regulations in 21 CFR 202.
5. Regulations on making changes in application in 21 CFR 314.70, 314.71, 314.72, 314.97, 314.99, and 601.12.
6. Regulations on reports in 21 CFR 314.80, 314.81, 600.80 and 600.81.
7. Local, state, and Federal environmental impact laws.

If this application applies to a drug product that the FDA has proposed for scheduling under the Controlled Substances Act I agree not to market the product until the Drug Enforcement Administration makes a final scheduling decision.

The data and information in this submission have been reviewed and, to the best of my knowledge are certified to be true and accurate.

Warning: a willfully false statement is a criminal offense, U.S. Code, title 18, section 1001.

SIGNATURE OF RESPONSIBLE OFFICIAL OR AGENT	TYPED NAME AND TITLE	DATE
P. Patel for SA	Shahid Ahmed, Vice President Regulatory Affairs, Ben Venue Labs.	3-1-01

ADDRESS *(Street, City, State, and ZIP Code)*	Telephone Number
270 Northfield Road, Bedford, Ohio 44146	(440) 201-3333

Public reporting burden for this collection of information is estimated to average 24 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Department of Health and Human Services
Food and Drug Administration
CBER, HFM-99
Rockville Pike
Rockville, MD 20852-1448

Food and Drug Administration
CDER, HFD-94
12420 Parklawn Dr., Room 3046
Rockville, MD 20852

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB 1401 control number.

FORM FDA 356h (4/00)

REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH

ANDA Number: 75-547 **Date of Submission: July 20, 1999**
Applicant's Name: Bedford Laboratories
Established Name: Thiotepa for Injection, 15 mg/vial

Labeling Deficiencies:
1. CONTAINER (1 mL vial)- Satisfactory.

2. CARTON (1 x 1 mL vial) - Satisfactory.

3. INSERT

a. DOSAGE AND ADMINISTRATION (Preparation of Solution)

Revise the table in this section back to being the same as the reference listed drug. See chemistry deficiency number C(2.).

b. REFERENCES- Include the following to appear as reference #7 and correct in the text of the insert:

7. OSHA Work-Practice Guidelines for Personnel Dealing with Cytotoxic (Antineoplastic) Drugs. *AM J Hosp Pharm* 1986;43:1193-1204.

Please revise your insert labeling, as instructed above, and submit 12 copies of final printed insert labeling.

Prior to approval, it may be necessary to further revise your labeling subsequent to approved changes for the reference listed drug. We suggest that you routinely monitor the following website for any approved changes: http://www.fda.gov/cder/ogd/rld/labeling_review_branch.html

To facilitate review of your next submission, and in accordance with 21 CFR 314.94(a)(8)(iv), please provide a side-by-side comparison of your proposed labeling with your last submission with all differences annotated and explained.

Robert L. West, M.S., R.Ph.
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH

ANDA Number: 75-547 Date of Submission: December 29, 1998

Applicant's Name: Bedford Laboratories

Established Name: Thiotepa for Injection, 15 mg/vial

Labeling Deficiencies:

1. GENERAL COMMENTS:

2. CONTAINER (1 mL vial)

   a. Include the route of administration as required by 21 CFR 201.100(b)(3).

3. CARTON (1 x 1 mL vial)

   a. See comment under CONTAINER.

4. INSERT

   a. TITLE

      We encourage the inclusion of "Rx only" in this section.

   b. DOSAGE AND ADMINISTRATION

      i. Preparation of Solution

         Revise the first sentence of paragraph three of this subsection to read as follows:

         In order to eliminate haze, filter solutions through a...

Please revise your container labels, carton labeling, and insert labeling, as instructed above, and submit 12 copies of final printed container labels, along with 12 copies of final printed carton and insert labeling.

Please note that we reserve the right to request further changes in your labels and/or labeling based upon changes in the approved labeling of the listed drug or upon further review of the application prior to approval.

To facilitate review of your next submission, and in accordance with 21 CFR 314.94(a)(8)(iv), please provide a side-by-side comparison of your proposed labeling with your last submission with all differences annotated and explained.

John J. Crawford

Robert L. West, M.S., R.Ph.
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

ESTABLISHMENT EVALUATION REQUEST
DETAIL REPORT

Application: ANDA 75547/000
Stamp: 31-DEC-1998
Regulatory Due:
Applicant: BEDFORD LABS
270 NORTHFIELD RD
BEDFORD, OH 44146
Priority:
Org Code: 600

Action Goal:
District Goal: 30-NOV-1999
Brand Name:
Estab. Name: THIOTEPA
Generic Name:

Dosage Form: (FOR INJECTION)
Strength: 15 MG VIAL

Application Comment:
FDA Contacts: D. HUIE (HFD-615) 301-827-5862 , Project Manager
M. SMELA JR (HFD-625) 301-827-5848 , Team Leader

Overall Recommendation:
Establishment: 1519257
BEN VENUE LABORATORIES INC
270 & 300 NORTHFIELD RD
BEDFORD, OH 441460568

DMF No: AADA:
Responsibilities: FINISHED DOSAGE MANUFACTURER
Profile: SVS OAI Status: NONE
Estab. Comment:

Milestone Name	Date	Req. Type	Insp. Date	Decision & Reason	Creator
SUBMITTED TO OC	09-FEB-1999				DAVISG

Establishment:

DMF No: 13911 AADA:
Responsibilities: DRUG SUBSTANCE MANUFACTURER
Profile: CSN OAI Status: NONE
Estab. Comment:

Milestone Name	Date	Req. Type	Insp. Date	Decision & Reason	Creator
SUBMITTED TO OC	09-FEB-1999				DAVISG